



Article of Interest

Law, M. Value of low dose combination treatment with blood pressure lowering drugs: analysis of 354 randomized trials. *British Medical Journal*. 2003. ([Click to Access](#))

Context and Study Objective

A common approach to treating hypertension involves initiating mono-therapy, up-titrating to full dose, and then adding a second agent. This article explores whether low dose combination therapy achieves similar blood pressure reductions but with lower side effect rates.

Main Outcome

Average blood pressure reduction and prevalence of adverse effects of anti-hypertensive agents when administered individually or in combination.

Design, Setting, and Participants

All double blind randomized controlled trials involving fixed doses of the five principal classes of anti-hypertensives—thiazides, β -blockers, ACEi, ARBs, CCBs—were identified. Trials involving patients with coronary artery disease/strokes were excluded. In aggregate, 354 trials with 60,000 patients were included.

Results

-Table: Half standard (mono-therapy) dosing achieved 80% of the blood pressure lowering effect of full dose therapy (N.B. BP reductions depicted as treated minus placebo, reductions in diastolics comparable). Among a heterogeneous population, the degree of BP reduction was similar between classes of agents.

-Mean BP reduction with full dose combination therapy (irrespective of agents) was 14.6/8.6 mm Hg; half standard dose combination therapy was 13.3/7.3 mm Hg.

-Figure: Among thiazides, CCBs, and β -blockers, side effects were dose dependent. ACEi/ARB related adverse effects (principally cough) were dose independent.

-Among all patients on mono-therapy (regardless of dose), 5.0% reported side effects. Among all patients on combination therapy (regardless of dose), 7.5% reported side effects.

Average Systolic Reduction (mm Hg) By Class		
	Half Dose	Full Dose
CCB	5.9	8.8
Thiazides	7.4	8.8
β -blockers	7.4	9.2
ACEi/ARB	7.4	9.4

Clinical Perspective

-Half standard dosing lowers both systolic and diastolic blood pressure by 80% of that seen with full dose therapy, yet with only a fraction of the side effects. Similarly, half standard dose combination therapy achieves nearly comparable reductions versus full dose combination therapy but with a markedly lower adverse effects rate.

-For patients with mild hypertension, I start with low dose combination therapy and up titrate as needed. Since countless agents are available as generic 2-in-1 formulations, the patient still only takes "one pill."

-Given the side effects from ACEi/ARBs are dose independent, these are the first agents I utilize at full dose.

-Perhaps limiting study generalizability, average patient age was 53 & those with cardio-vascular events were excluded.

